

Claims

1. Use of perfluoroalkyl-containing metal complexes that have a critical micelle formation concentration $< 10^{-3}$ mol/l, a hydrodynamic micelle diameter ($2 R_h$) > 1 nm and a proton relaxivity in plasma (R_1) > 10 l/mmol's as contrast media in MR imaging for visualization of plaque.

2. Use according to claim 1, characterized in that the metal complexes are also used as MRI contrast media for visualization of lymph nodes.

3. Use according to claim 1 or 2, wherein the metal complexes are also used as MRI contrast media for visualization of infarcted and necrotic tissue.

4. Use according to one of claims 1 to 3, wherein the metal complexes are also used as MRI contrast media for independent visualization of necroses and tumors.

5. Use according to claim 1, wherein metal complexes whose micelle formation concentration is $< 10^{-4}$ mol/l are used.

6. Use according to claim 1, wherein metal complexes whose hydrodynamic micelle diameter is ≥ 3 , preferably > 4 nm, are used.

7. Use according to claim 1, wherein metal complexes that have a proton relaxivity in plasma of > 13 l/mmol's, preferably > 15 l/mmol's, are used.

8. Use according to one of claims 1 to 7, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula I

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Sld
AR

R^F-L-K

I

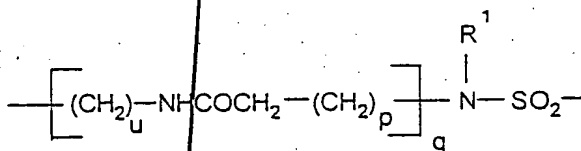
in which

R^F is a perfluorinated, straight-chain or branched carbon chain with formula -C_nF_{2n}E, in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom and n stands for numbers 4-30,



L means a direct bond, a methylene group, an -NHCO group, a group



(Please change R¹ to R^a in the formula!)

whereby p means the numbers 0 to 10, and q and n,

independently of one another, mean numbers 0 or 1, and

R³ is a hydrogen atom, a methyl group, a -CH₂-OH group, a -CH₂-CO₂H group or a C₂-C₁₅ chain, which optionally is interrupted by 1 to 3 oxygen atoms, 1 to 2 >CO groups or an optionally substituted aryl group and/or is substituted with 1 to 4 hydroxyl groups, 1 to 2 C₁-C₄ alkoxy groups, 1 to 2 carboxy groups, a group -SO₃H-,

or is a straight-chain, branched, saturated or unsaturated C₂-C₃₀ carbon chain, which optionally contains 1 to 10 oxygen atoms, 1 to 3 -NR^a groups, 1 to

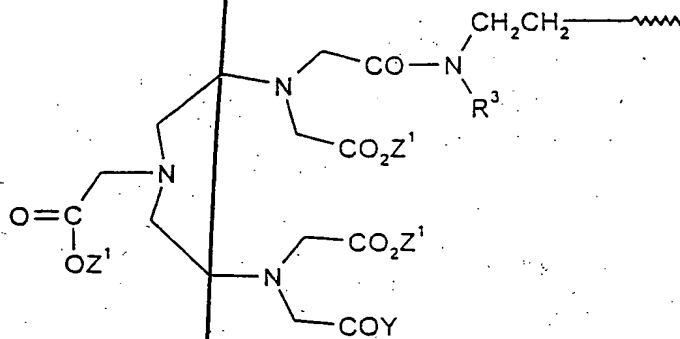
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2 sulfur atoms, a piperazine, a $-\text{CONR}^a$ group, an $-\text{NR}^a\text{CO}$ group, an $-\text{SO}_2$ group, an $-\text{NR}^a-\text{CO}_2$ group, 1 to 2 CO groups, a group $-\text{CO}-\text{N}-\text{T}-\text{N}(\text{R}^a)-\text{SO}_2-\text{R}^F$, or 1 to 2 optionally substituted aryls and/or is interrupted by these groups and/or is optionally substituted with 1 to 3 $-\text{OR}^a$ groups, 1 to 2 oxo groups, 1 to 2 $-\text{NH}-\text{COR}^a$ groups, 1 to 2 $-\text{CONHR}^a$ groups, 1 to 2 $-(\text{CH}_2)_p-\text{CO}_2\text{H}$ groups, 1 to 2 groups $-(\text{CH}_2)_p-(\text{O})_q-\text{CH}_2\text{CH}_2-\text{R}^F$, whereby

R^a , R^F and p and q have the above-indicated meanings, and

T means a C_2-C_{10} chain, which optionally is interrupted by 1 to 2 oxygen atoms or 1 to 2 $-\text{NHCO}$ groups,

K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides, specifically for a complexing agent or complex of general formula II



(II)

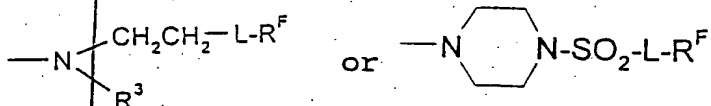
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in which R^c , R^1 and B are independent of one another,
and

R^c has the meaning of R^a or means $-(CH_2)_m-L-R^F$,
whereby m is 0, 1 or 2, and L and R^F have the
above-mentioned meaning,

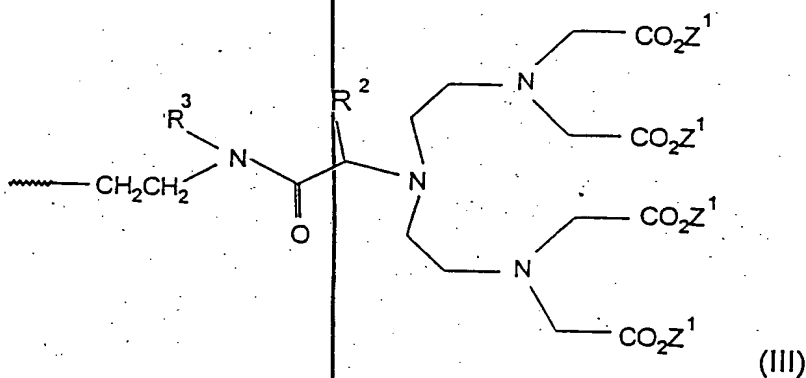
R^1 , independently of one another, mean a hydrogen atom
or a metal ion equivalent of atomic numbers 22-29,
42-46 or 58-70,

B means $-OR^1$ or



whereby R^1 , L, R^F and R^c have the above-mentioned
meanings, or

K stands for a complexing agent or complex of general
formula III

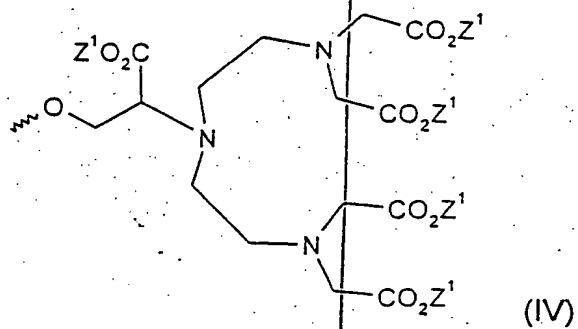


in which R^c and R^1 have the above-mentioned meanings
and R^b has the meaning of R^a

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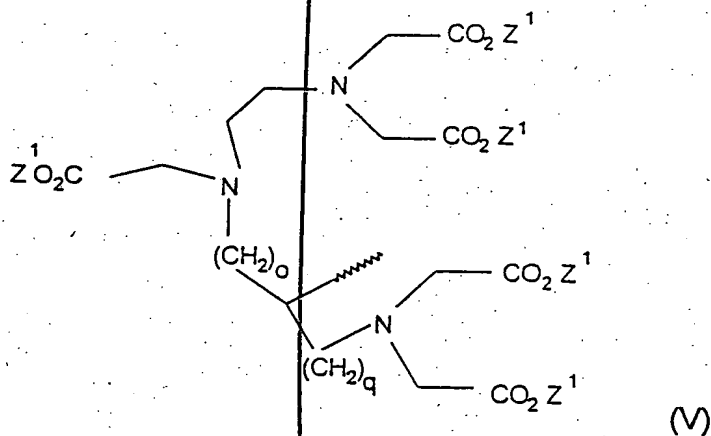
or

K stands for a complexing agent or complex of general formula IV



in which R¹ has the above-mentioned meaning
or

K stands for a complexing agent or complex of general formula V

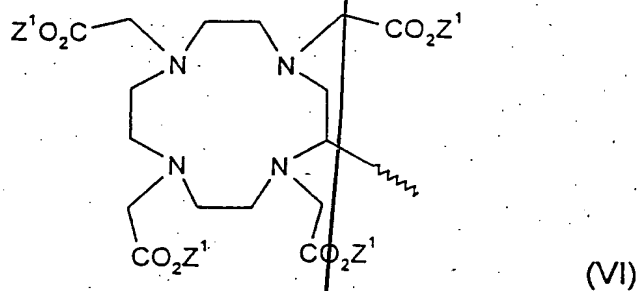


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in which R^1 has the above-mentioned meaning, and o and q stand for numbers 0 or 1, and yields the sum $o + q = 1$,

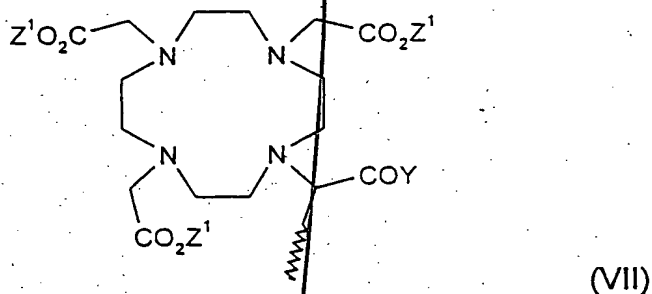
or

K stands for a complexing agent or complex of general formula VI



in which R^1 has the above-mentioned meaning
or

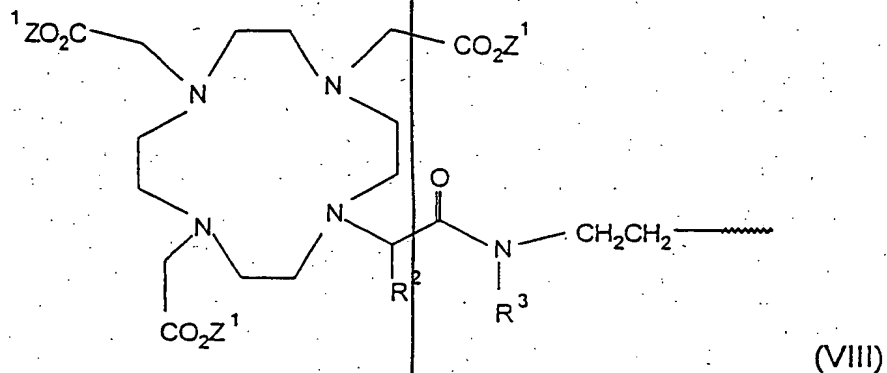
K stands for a complexing agent or complex of general formula VII



in which R^1 and B have the above-mentioned meanings
or

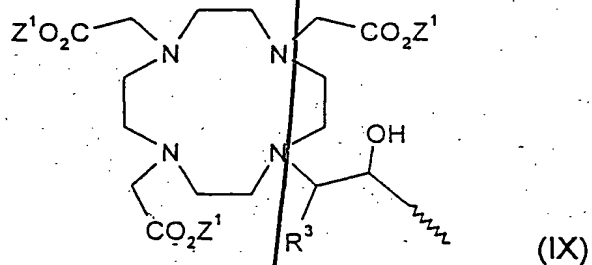
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K stands for a complexing agent or complex of general formula VIII



in which R^c and R^1 have the above-mentioned meanings,
and R^b has the above-mentioned meaning of R^a
or

K stands for a complexing agent or complex of general formula IX

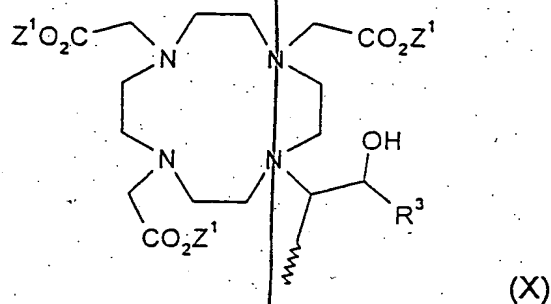


in which R^c and R^1 have the above-mentioned meanings,
or

K stands for a complexing agent or complex of general

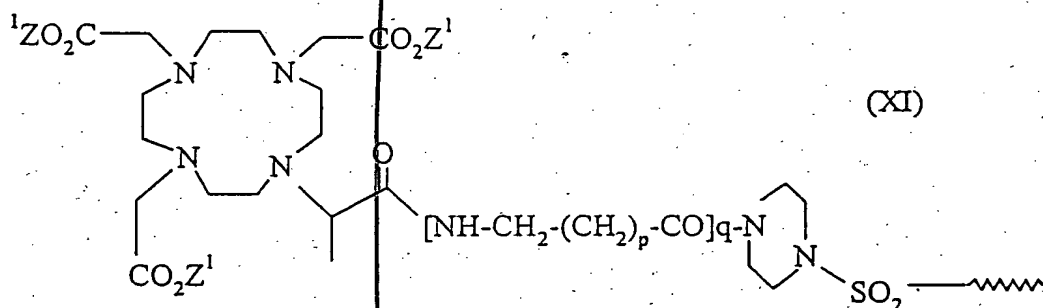
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formula X



in which R^c and R^1 have the above-mentioned meanings,
or

stands for a complexing agent or complex of general
formula XI

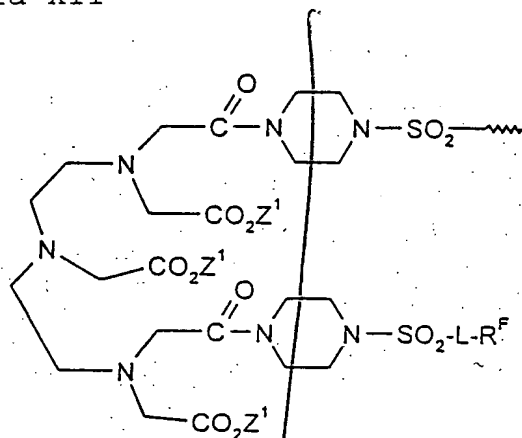


in which R^1 , p and q have the above-mentioned meanings,
and R^b has the meaning of R^a ,

or

K stands for a complexing agent or complex of general

formula XII

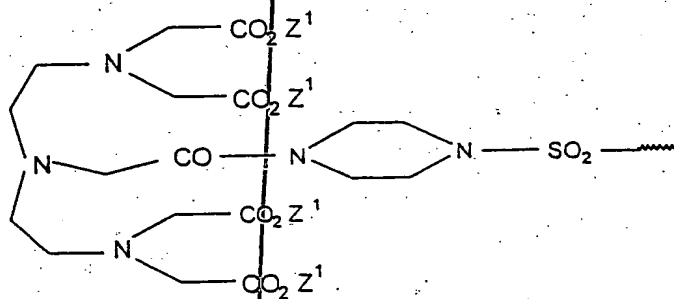


(XII)

in which L, R^F and Z¹ have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XIII

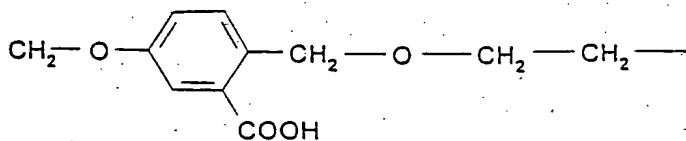
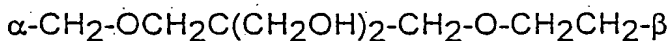
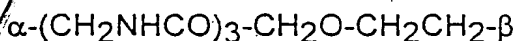
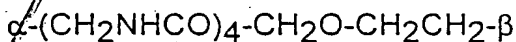
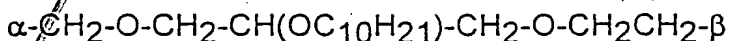
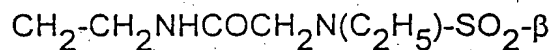
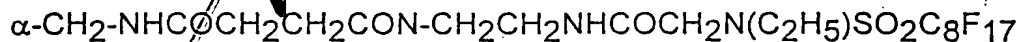
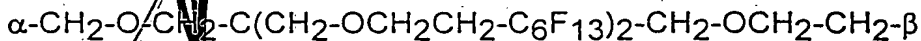
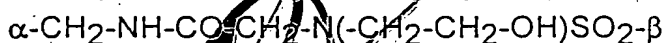
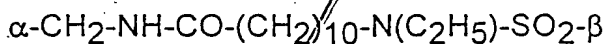
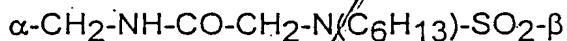
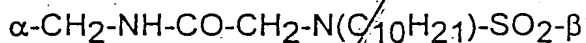
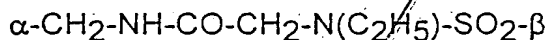
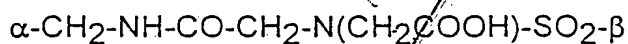
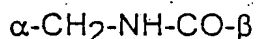
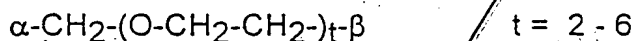
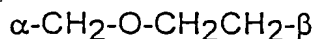
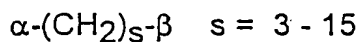
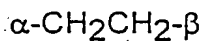
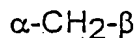


(XIII)

in which R¹ has the above-mentioned meaning,
are used.

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9. Use according to claim 8, wherein the compounds of general formula I, in which L stands for

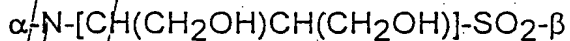
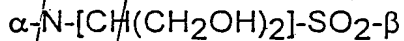
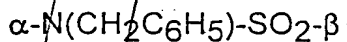
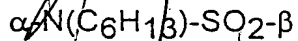
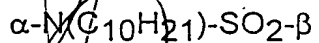
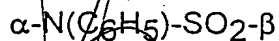
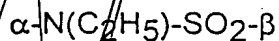
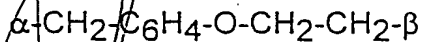
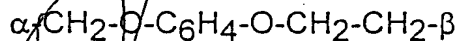
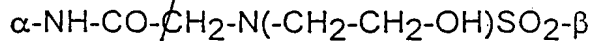
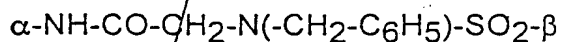
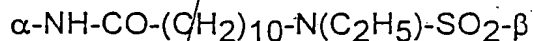
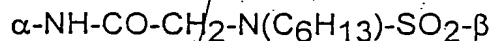
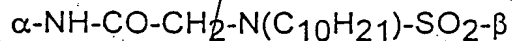
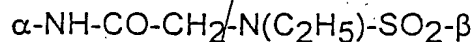
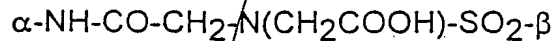
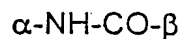
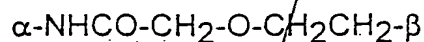
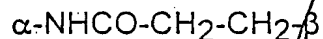
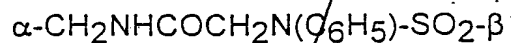


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and in which α represents the binding site to the complexing agent or metal complex K, and β represents the binding site to the fluorine radical, are used.

10. Use according to claim 8 or 9, wherein the compounds of formula I in which n in formula $-C_nF_{2n}E$ stands for numbers 4-15 and/or E in this formula means a fluorine atom are used.

11. Use according to one of claims 8 to 10, wherein the following compounds are used:

- Gadolinium complex of 10-[1-methyl-2-oxo-3-aza-5-oxo-{4-perfluorooctylsulfonyl-piperazin-1-yl}-pentyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17-heptafluoroheptadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5,9-dioxo-9-{4-perfluorooctyl}-piperazin-1-yl]-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctyl-sulfonyl)-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-oxa-1H,1H,2H,3H,3H,5H,5H,6H,6H-perfluorotetradecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19-henicosafuoro-nonadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

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- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-11-aza-11-(perfluorooctylsulfonyl)-tridecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-8-phenyl-octyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraaza-cyclododecane.

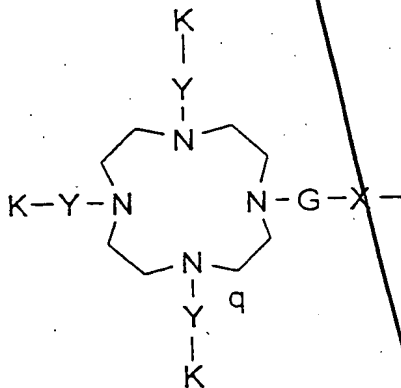
12. Use according to one of claims 1-7, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ia



in which

- A is a molecule part that contains 2 to 6 metal complexes, which are bonded directly or via a linker to a nitrogen atom of an annular skeleton chain, and
- R^F is a perfluorinated, straight-chain or branched carbon chain with formula $-C_nF_{2n}E$, in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

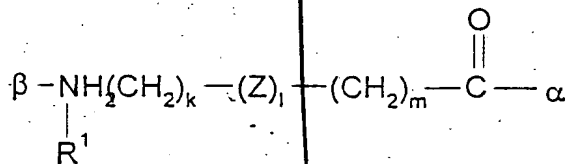
whereby molecule part A has the following structure:



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whereby

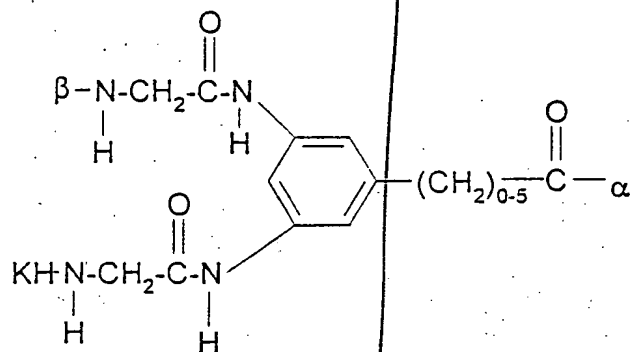
- o q^1 is a number 0, 1, 2 or 3,
- o K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides,
- o X is a direct bond to the perfluoroalkyl group, a phenylene group or a C_1 - C_{10} alkylene chain, which optionally contains 1-15 oxygen atoms, 1-5 sulfur atoms, 1-10 carbonyl groups, 10-10 (NR^d) groups, 1-2 NR^dSO_2 groups, 1-10 $CONR^d$ groups, 1 piperidine group, 1-3 SO_2 groups and 1-2 phenylene groups or optionally is substituted by 1-3 radicals R^F , in which R^d stands for a hydrogen atom, a phenyl group, benzyl group or a C_1 - C_{15} alkyl group, which optionally contains 1-2 $NHCO$, 1-2 CO groups, 1-5 oxygen atoms and optionally is substituted by 1-5 Hydroxy, 1-5 methoxy, 1-3 carboxy, or 1-3 R^F radicals,
- o V is a direct bond or a chain of general formula IIa or IIIa:



(IIa)

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B



(IIIa)

in which

- R^e is a hydrogen atom, a phenyl group, a benzyl group or a C_1 - C_7 alkyl group, which optionally is substituted with a carboxy group, a methoxy group or a hydroxy group,
- W is a direct bond, a polyglycol ether group with up to 5 glycol units, or a molecule part of general formula IVa



in which R^h is a C_1 - C_7 carboxylic acid, a phenyl group, a benzyl group or a $-(CH_2)_{1-5}-NH-K$ group,

- α represents the binding to the nitrogen atom of the skeleton chain, β represents the binding to complexing agents or metal complex K ,
- and in which variables k and m stand for natural numbers between 0 and 10, and l stands for 0 or 1

and whereby

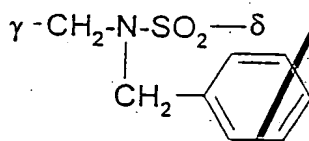
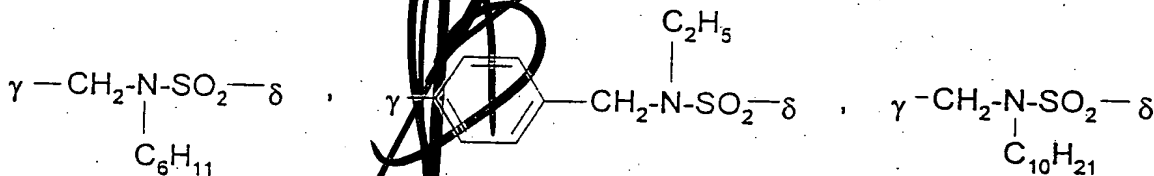
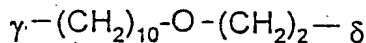
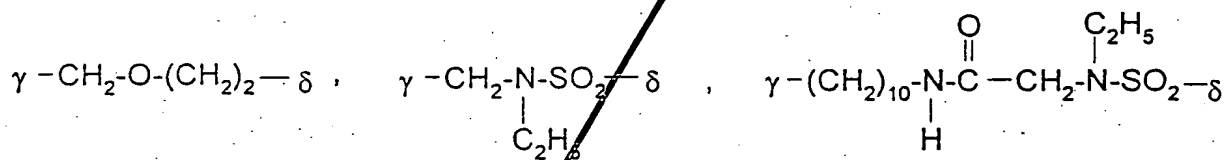
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12

AB
 D is a CO or SO₂ group,
 are used.

13. Use according to claim 12, wherein the compounds of general formula Ia in which q is the number 1 are used.

14. Use according to claim 12, wherein the compounds of general formula Ia are used, in which molecule part X is an alkylene chain, which contains 1-10 CH₂CH₂O groups or 1-5 COCH₂NH groups, a direct bond or one of the following structures

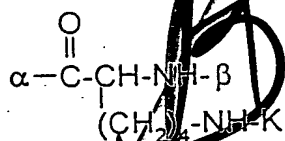
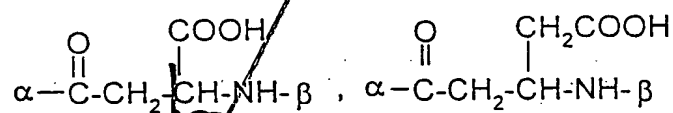
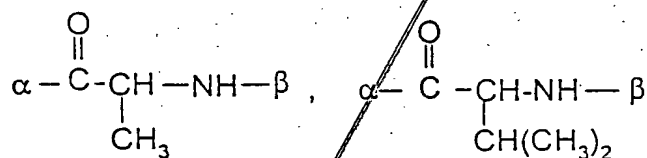
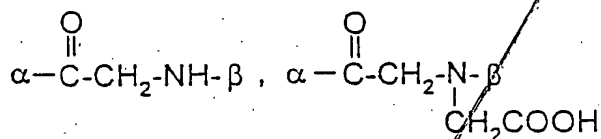


whereby

γ binds to D, and δ binds to R^F.

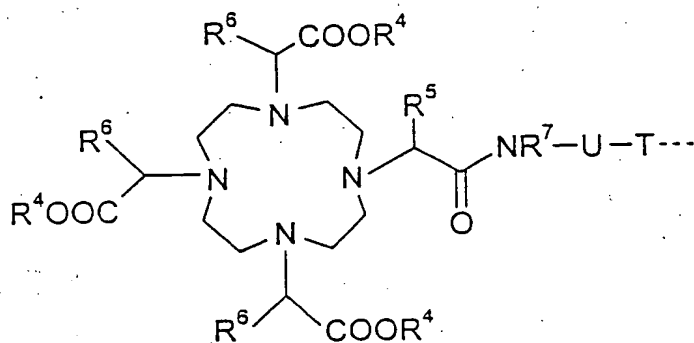
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15. Use according to claim 12, wherein the compounds of general formula Ia, in which V is a molecule part with one of the following structures

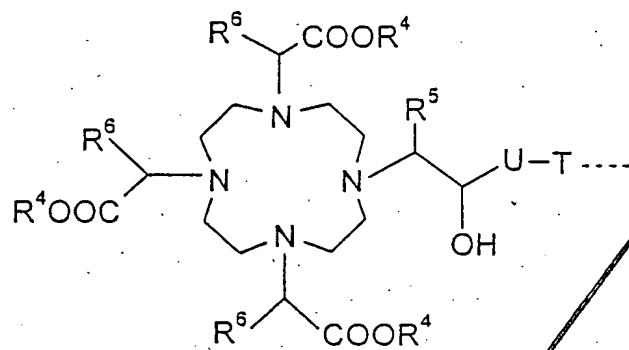


are used.

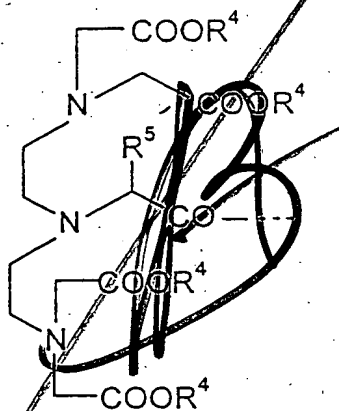
16. Use according to claim 12, wherein the compounds of general formula Ia, in which K represents a complex of general formula Va, VIa, VIIa or VIIIa,



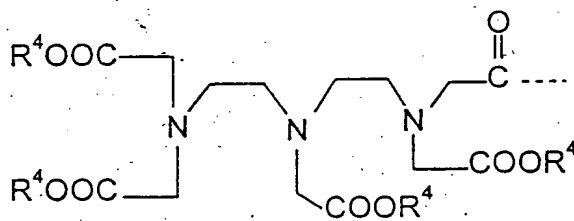
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(VIa)



(VIIa)



(VIIIa)

are used,
whereby

R^1 , independently of one another, are a hydrogen atom or a metal ion equivalent of the elements of atomic numbers 23-29, 42-46 or 58-70,

- R^8 is a hydrogen atom or a straight-chain, branched, saturated or unsaturated C_1 - C_{30} alkyl chain, which optionally is substituted by 1-5 hydroxy, 1-3 carboxy or 1 phenyl group(s) and/or optionally is interrupted by 1-10 oxygen atoms, 1 phenylene group or 1 phenylenoxy group,
- R^6 is a hydrogen atom, a straight-chain or branched C_1 - C_7 alkyl radical, a phenyl radical or benzyl radical,
- R^7 is a hydrogen atom, a methyl group or ethyl group, which optionally is substituted by a hydroxy group or carboxy group,
- U^3 is a straight-chain, branched, saturated or unsaturated C_1 - C_{20} alkylene group optionally containing 1-5 imino groups, 1-3 phenylene groups, 1-3 phenylenoxy groups, 1-3 phenylenimino groups, 1-5 amide groups, 1-2 hydrazide groups, 1-5 carbonyl groups, 1-5 ethylenoxy groups, 1 urea group, 1 thiourea group, 1-2 carboxyalkylimino groups, 1-2 ester groups, 1-1-0 oxygen atoms, 1-5 sulfur atoms and/or 1-5 nitrogen atoms, and/or optionally substituted by 1-5 hydroxy groups, 1-2 mercapto groups, 1-5 oxo groups, 1-5 thioxo groups, 1-3 carboxy groups, 1-5 carboxyalkyl groups, 1-5 ester groups and/or 1-3 amino groups, whereby the optionally contained phenylene groups can be

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substituted by 1-2 carboxy groups, 1-2 sulfone groups or 1-2 hydroxy groups

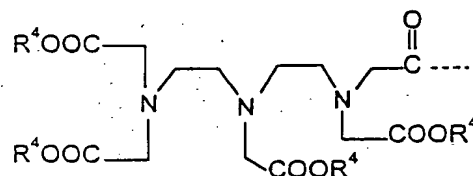
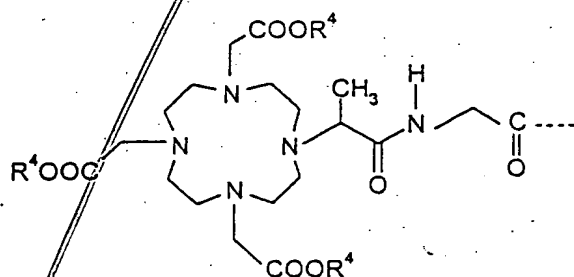
- T^1 stands for a $-\text{CO}-\beta$, $-\text{NHCO}-\beta$ or $-\text{NHCS}-\beta$ group, whereby β represents the binding site to V,

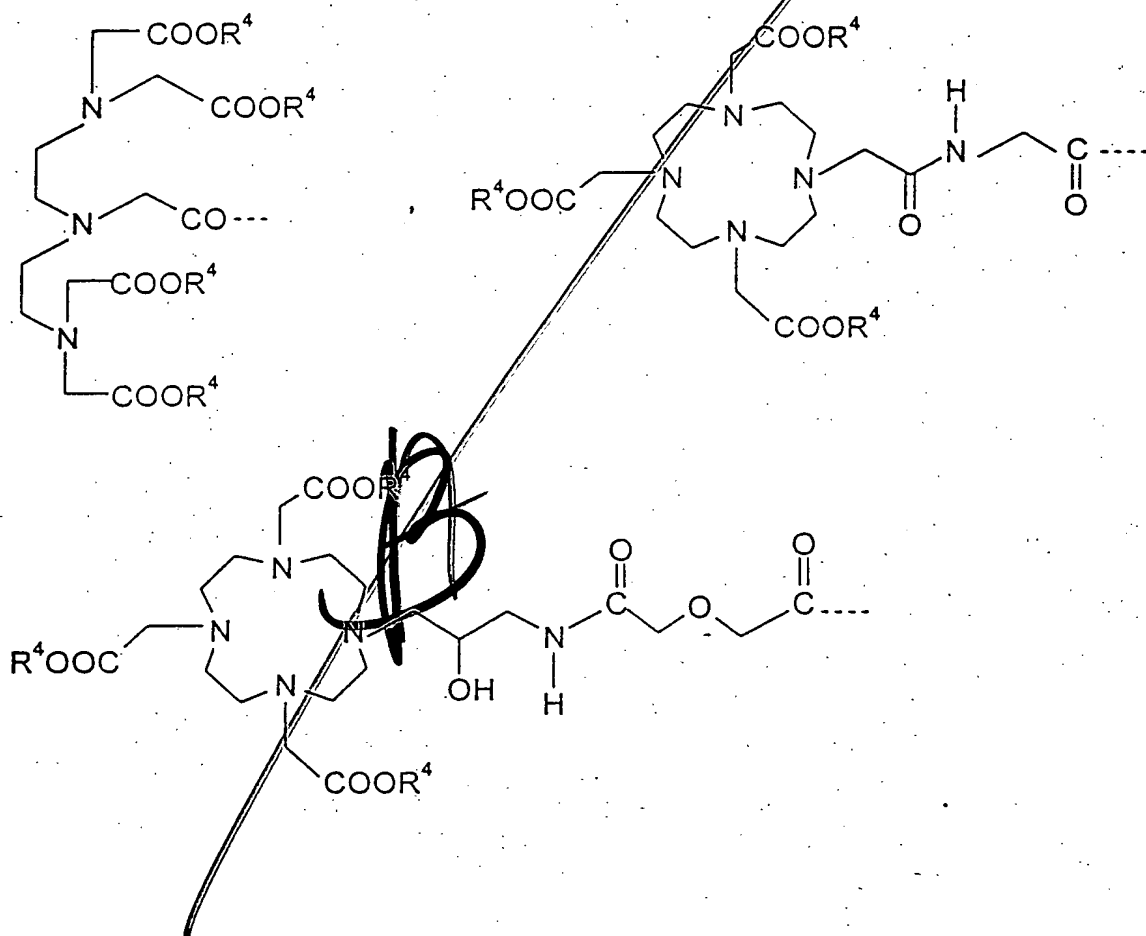
are used.

17. Use according to claim 16, wherein the $\text{C}_1\text{-C}_{20}$ alkylene chain that stands for U^3 contains the groups $-\text{CH}_2\text{NHCO}-$, $-\text{NHCOCH}_2\text{O}-$, $-\text{NHCOCH}_2\text{OC}_6\text{H}_4-$, $-\text{N}(\text{CH}_2\text{CO}_2\text{H})-$, $-\text{CH}_2\text{OCH}_2-$, $-\text{NHCOCH}_2\text{C}_6\text{H}_4-$, $-\text{NHCSNHC}_6\text{H}_4-$, $-\text{CH}_2\text{OC}_6\text{H}_4-$, $-\text{CH}_2\text{CH}_2\text{O}-$ and/or is substituted by the groups $-\text{COOH}$ and $-\text{CH}_2\text{COOH}$.

18. Use according to claim 16, wherein U^3 stands for a $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{C}_6\text{H}_4-$, $-\text{C}_6\text{H}_{10}-$, $-\text{CH}_2\text{C}_6\text{H}_4-$, $-\text{CH}_2\text{NHCOCH}_2\text{CH}(\text{CH}_2\text{CO}_2\text{H})-\text{C}_6\text{H}_4-$, $-\text{CH}_2\text{NHCOCH}_2\text{OCH}_2-$, $-\text{CH}_2\text{NHCOCH}_2\text{C}_6\text{H}_4-$ group.

19. Use according to claim 12, wherein the compounds of general formula Ia in which K has one of the following structures:





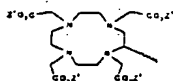
are used.

20. Use according to one of claims 12 to 19, wherein the compounds of general formula Ia in which the perfluoroalkyl chain is R^F - C_6F_{13} , - C_8F_{17} , - $C_{10}F_{21}$ or - $C_{12}F_{25}$ are used.

21. Use according to one of claims 12 to 20, wherein the gadolinium complex of 1,4,7-tris{1,4,7-tris(N-(carboxylatomethyl)-10-[N-1-methyl-3,6-diaza-2,5,8-trioxooctane-1,8-diyl)]-1,4,7,10-tetraazacyclododecane, Gd complex}-10-[N-

2H, 2H, 4H, 4H, 5H, 5H-3-oxa-perfluorotridecanoyl]-1,4,7,10-tetraazacyclododecane is used.

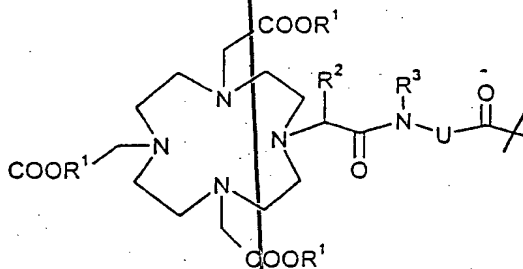
22. Use according to one of claims 1 to 7, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ib



(Ib)

in which

K means a complexing agent or a metal complex of general formula IIb



(IIb)

whereby

R¹ stands for a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70,

R² and R³ stand for a hydrogen atom, a C₁-C₇ alkyl group, a benzyl group, a phenyl group, -CH₂OH or -CH₂-OCH₃,

U^2 stands for radical L^1 , whereby L^1 and U^2 , independently of one another, can be the same or different,

A^1 means a hydrogen atom, a straight-chain or branched C_1 - C_{30} alkyl group, which optionally is interrupted by 1-15 oxygen atoms, and/or optionally is substituted with 1-10 hydroxy groups, 1-2 COOH groups, a phenyl group, a benzyl group and/or 1-5 $-OR^9$ groups, with R^9 in the meaning of a hydrogen atom or a C_1 - C_7 alkyl radical, or $-L^1-R^F$,

L^1 means a straight-chain or branched C_1 - C_{30} alkylene group, which optionally is interrupted by 1-10 oxygen atoms, 1-5 $-NH-CO$ groups, 1-5 $-CO-NH$ groups, by a phenylene group optionally substituted by a COOH-group, 1-3 sulfur atoms, 1-2 $-N(B^1)-SO_2$ groups and/or 1-2 $-SO_2-N(B^1)-$ groups with B^1 in the meaning of A^1 , an NHCO group, a CONH group, an $N(B^1)-SO_2$ group or an $-SO_2-N(B^1)$ group and/or optionally is substituted with radical R^F , and

R^F means a straight-chain or branched perfluorinated alkyl radical of formula $C_nF_{2n}E$,

whereby n stands for number 4-30, and

E stands for a terminal fluorine atom, chlorine atom, bromine atom, iodine atom or a hydrogen atom,

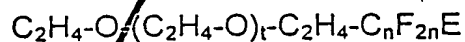
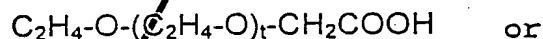
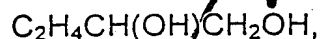
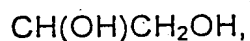
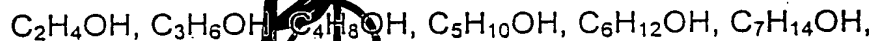
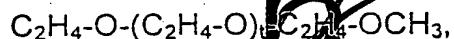
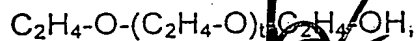
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and optionally present acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides, are used.

23. Use according to claim 22, wherein the compounds of general formula Ib, in which R^2 , R^3 and R^9 , independently of one another, mean hydrogen or a C_1 - C_4 alkyl group, are used.

24. Use according to claim 22, wherein the compounds of general formula Ib, in which A^1 means hydrogen, a C_1 - C_5 alkyl radical,

the radicals



or

whereby

s stands for integers 1 to 15,

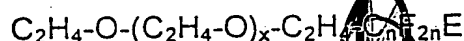
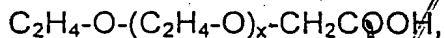
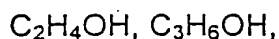
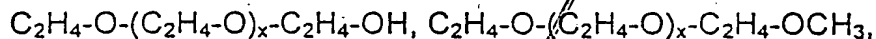
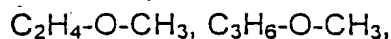
t stands for integers 0 to 13,

u^1 stands for integers 1 to 10,

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n stands for integers 4 to 20, and
 E stands for hydrogen, fluorine, chlorine, bromine or
 iodine atoms, and if necessary, their branched isomers,
 are used.

25. Use according to claim 22, wherein the compounds of
 general formula Ib, in which A¹ means hydrogen, C₁-C₁₀ alkyl,



whereby

x stands for integers 0 to 5,

y stands for integers 1 to 6,

w stands for integers 1 to 10,

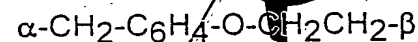
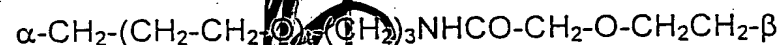
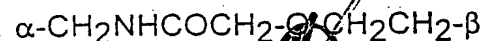
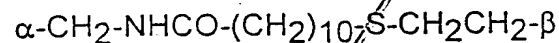
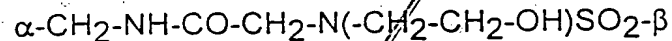
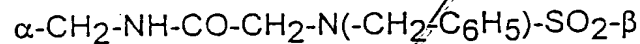
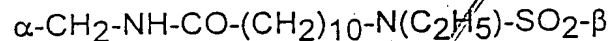
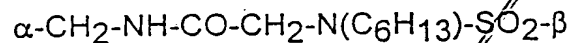
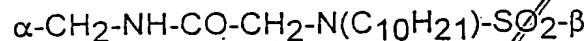
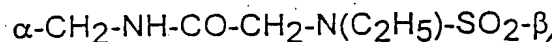
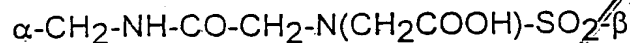
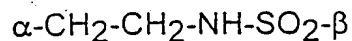
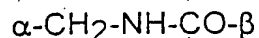
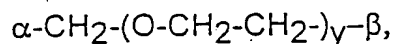
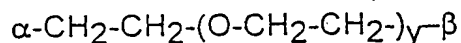
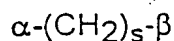
n stands for integers 4 to 15, and

E stands for a fluorine atom, and, if necessary, their
 branched isomers

are used.

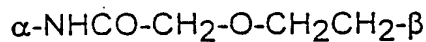
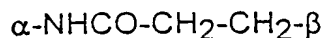
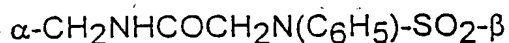
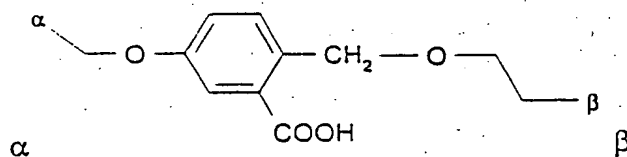
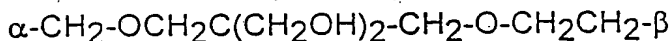
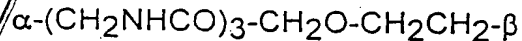
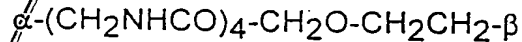
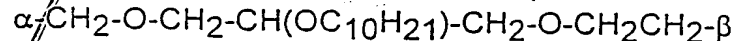
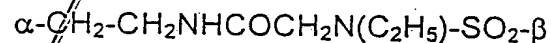
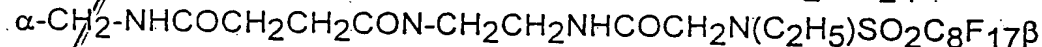
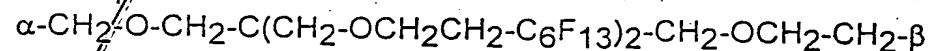
26. Use according to claim 22, wherein the compounds of
 general formula Ib, in which L¹ means

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whereby phenylene group 1,4 or

1,3 is linked



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α -NH-CO- β
 α -NH-CO-CH₂-N(CH₂COOH)-SO₂- β
 α -NH-CO-CH₂-N(C₂H₅)-SO₂- β
 α -NH-CO-CH₂-N(C₁₀H₂₁)-SO₂- β
 α -NH-CO-CH₂-N(C₆H₁₃)-SO₂- β
 α -NH-CO-(CH₂)₁₀-N(C₂H₅)-SO₂- β
 α -NH-CO-CH₂-N(-CH₂-C₆H₅)-SO₂- β
 α -NH-CO-CH₂-N(-CH₂-CH₂-OH)-SO₂- β
 α -NH-CO-CH₂- β
 α -CH₂-O-C₆H₄-O-CH₂-CH₂- β
 α -CH₂-C₆H₄-O-CH₂-CH₂- β
 α -N(C₂H₅)-SO₂- β
 α -N(C₆H₅)-SO₂- β
 α -N(C₁₀H₂₁)-SO₂- β
 α -N(C₆H₁₃)-SO₂- β
 α -N(C₂H₄OH)-SO₂- β
 α -N(CH₂COOH)-SO₂- β
 α -N(CH₂C₆H₅)-SO₂- β
 α -N-[CH(CH₂OH)₂]-SO₂- β
 α -N-[CH(CH₂OH)CH(OH)(CH₂OH)]-SO₂- β

whereby

s stands for integers 1 to 15 and

y stands for integers 1 to 6,

are used.

27. Use according to claim 22, wherein the compounds of general formula Ib, in which L¹ means

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α -CH₂-O-CH₂CH₂- β ,
 α -CH₂-CH₂-(O-CH₂-CH₂)_y- β ,
 α -CH₂-(O-CH₂-CH₂)_y- β ,
 α -CH₂-CH₂-NH-SO₂- β , Bsp. 10
 α -CH₂NHCOCH₂-O-CH₂CH₂- β ,
 α -CH₂-CH₂NHCOCH₂-O-CH₂CH₂- β ,
 α -CH₂-(CH₂-CH₂-O)_y-(CH₂)₃NHCO-CH₂-O-CH₂CH₂- β ,
 α -CH₂NHCO(CH₂)₁₀-O-CH₂CH₂- β ,
 α -CH₂CH₂NHCO(CH₂)₁₀-O-CH₂CH₂- β ,
 α -CH₂-O-CH₂-CH(OC₁₀H₂₁)-CH₂-O-CH₂CH₂- β ,
 α -CH₂-O-C₆H₄-O-CH₂-CH₂- β or
 α -CH₂-C₆H₄-O-CH₂-CH₂- β

whereby

y stands for integers 1 to 6,
are used.

28. Use according to claim 22, wherein the compounds of general formula Ib, in which R^F means a straight-chain or branched perfluorinated alkyl radical of formula C_nF_{2n}E, whereby n stands for number 4 to 15 and E stands for a terminal fluorine atom,
are used.

29. Use according to one of claims 22 to 28, wherein the following compounds are used:

- 1,4,7-Tris(carboxylatomethyl)-10-(3-aza-4-oxo-hexan-5-ylidic)-acid-(2,3-dihydroxypropyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide]-1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-{(3-aza-4-oxo-hexan-5-ylidic)acid-N-(3,6,9,12,15-pentaoxa)-hexadecyl)-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-

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AS1

amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex

-- 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-ylidene)-acid-N-5-hydroxy-3-oxa-pentyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex

-- 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-ylidene)-acid-[N-3,6,9,15-tetraoxa-12-aza-15-oxo-C₁₇-C₂₆-hepta-decafluoro)hexacosyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex

-- 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-ylidene)-acid-N-(2-methoxyethyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex.

30. Use according to one of claims 1 to 7, wherein as perfluoroalkyl-containing metal complexes, the compounds with sugar radicals of general formula Ic



in which

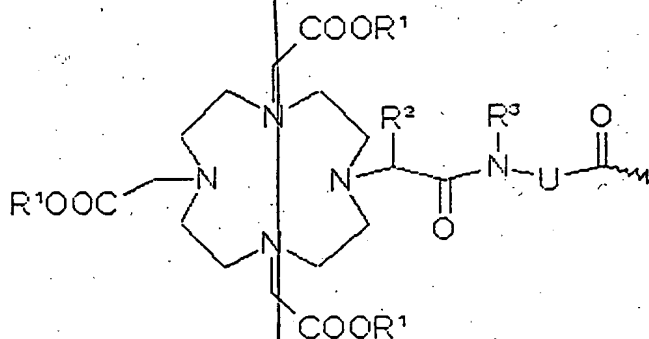
R represents a mono- or oligosaccharide radical bonded by the 1-OH- or 1-SH-position,

R^F is a perfluorinated, straight-chain or branched carbon chain with the formula -C_nF_{2n}E, in which E represents a

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terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

K stands for a metal complex of general formula IIc,



(IIc)

in which

R^1 means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two R^1 stand for metal ion equivalents,

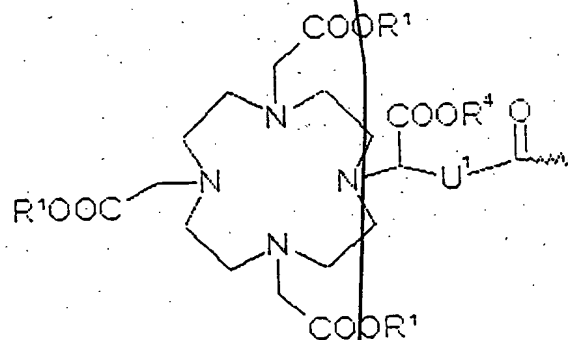
R^2 and R^3 , independently of one another, represent hydrogen, C_1 - C_7 alkyl, benzyl, phenyl, $-CH_2OH$ or $-CH_2OCH_3$, and

U represents $-C_6H_4-O-CH_2-\omega$, $-(CH_2)_{1-5}-\omega$, a phenylene group, $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega$, $-C_6H_4-(OCH_2CH_2)_{0-1}-N(CH_2COOH)-CH_2-\omega$, or a C_1 - C_{12} alkylene group or C_7 - C_{12} - C_6H_4-O group optionally interrupted by one or more oxygen atoms, 1 to 3 $-NHCO$ groups or 1 to 3 $-CONH$ groups and/or substituted with 1 to 3 $-(CH_2)_{0-5} COOH$ groups, whereby ω stands for the binding site to $-CO-$,

or

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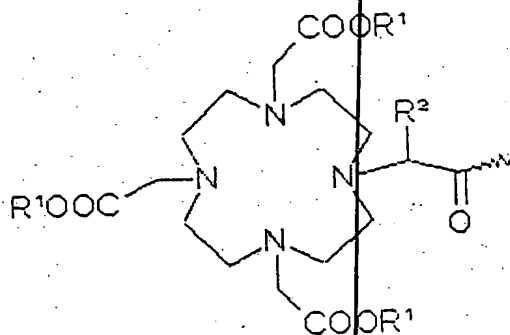
of general formula IIIc



(IIIc)

in which R¹ has the above-mentioned meaning, R⁴ represents hydrogen or a metal ion equivalent mentioned under R¹, and U¹ represents -C₆H₄-O-CH₂-ω, whereby ω means the binding site to -CO-

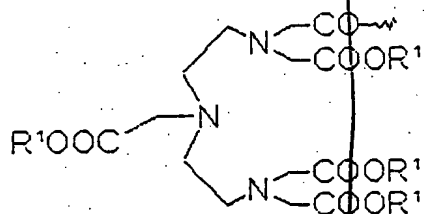
or of general formula IVc



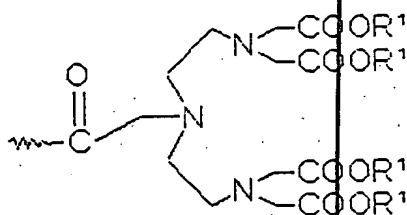
(IVc)

in which R¹ and R² have the above-mentioned meaning

or of general formula VcA or VcB



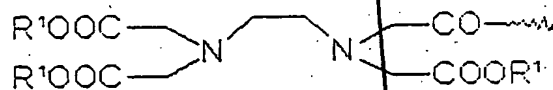
(VcA)



(VcB)

in which R¹ has the above-mentioned meaning,

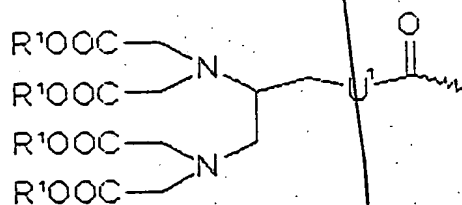
or of general formula VIc



(VIc)

in which R¹ has the above-mentioned meaning,

or of general formula VIIc

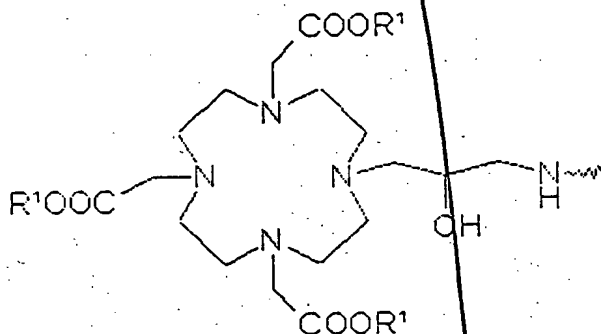


(VIIc)

in which R¹ has the above-mentioned meaning, and

U¹ represents -C₆H₄-O-CH₂-ω, whereby ω means the binding site to -CO-

or of general formula VIIIc



(VIIIc)

in which R¹ has the above-mentioned meaning,

and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

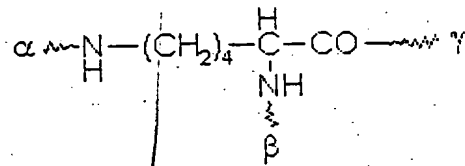
G for the case that K means metal complexes IIc to VIc represents a radical that is functionalized in at least three places and is selected from the following radicals a) to j)

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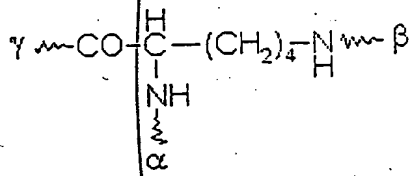
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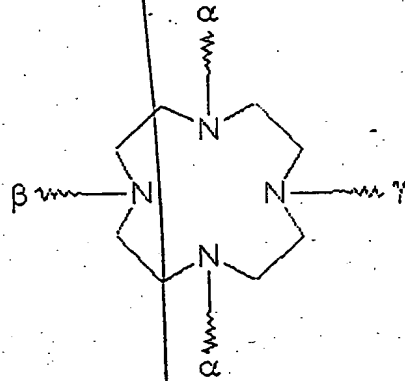
(a)



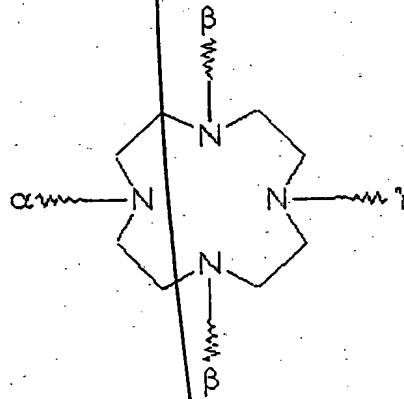
(b)



(c)

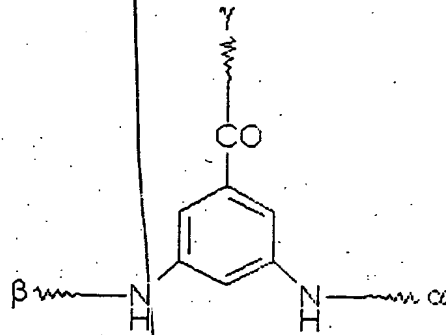


(d)

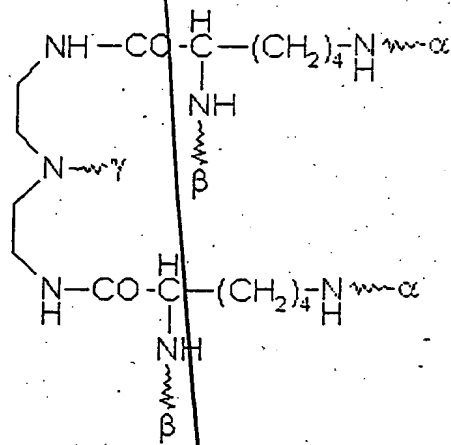


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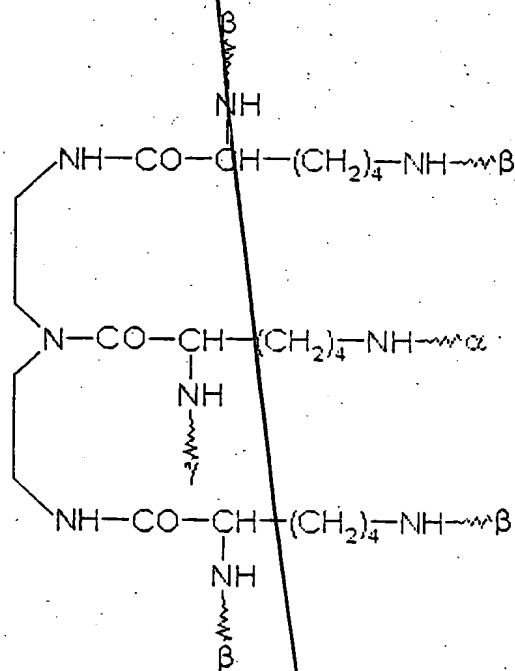
(e)



(f)



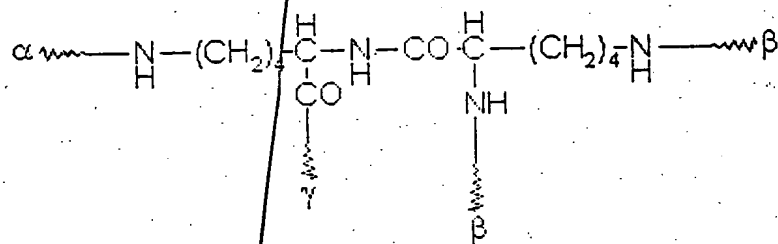
(g)



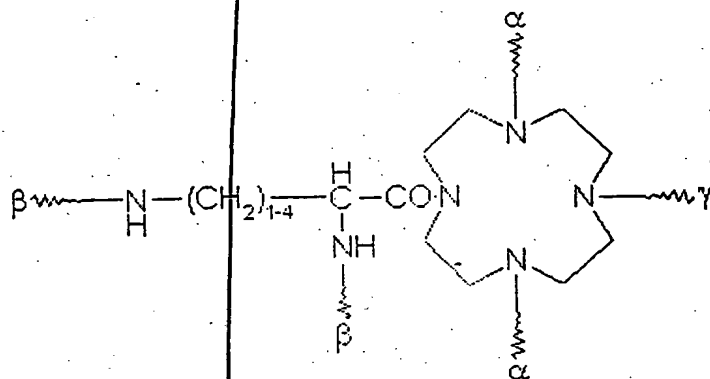
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RS

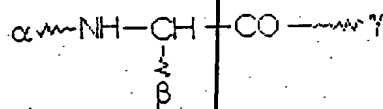
(h)



(i)



(j)

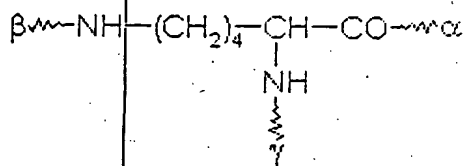


and

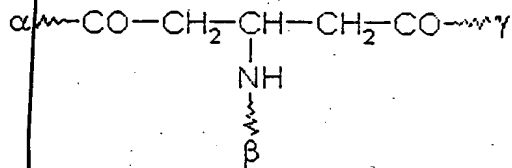
G for the case that K means metal complex VIIIC represents a radical that is functionalized in at least three places and is selected from k) or l),

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(k)



(l)

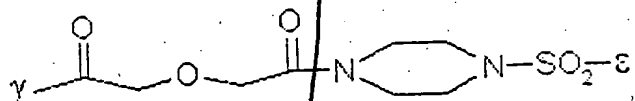
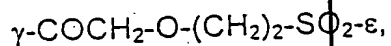
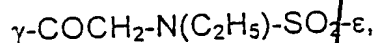


whereby α means the binding site of G to complex K, β is the binding site of G to radical Y, and γ represents the binding site of G to radical Z,

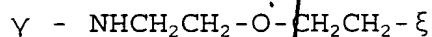
Y means $-\text{CH}_2$, $\delta - (\text{CH}_2)_{(1-5)} \text{CO} - \beta$, $\delta - \text{CH}_2 - \text{CHOH} - \text{CO} - \beta$ or $\delta - \text{CH}(\text{CHOH} - \text{CH}_2\text{OH}) - \text{CHOH} - \text{CHOH} - \text{CO} - \beta$, whereby δ represents the binding site to sugar radical R and β is the binding site to radical G,

Z stands for

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or



whereby γ represents the binding site of Z to radical G, and ξ means the binding site of Z to perfluorinated radical R^{F}

and

l^1 , m^1 , independently of one another, mean integers 1 or 2,

and

p^1 means integers 1 to 4,

are used.

31. Use according to claim 30, wherein the compounds of general formula Ic, in which R represents a monosaccharide radical with 5 to 6 C atoms or its deoxy compound, preferably glucose, mannose or galactose, are used.

32. Use according to claim 30, wherein the compounds of general formula Ic, in which R^2 and R^3 , independently of one another, mean hydrogen or C_1 - C_4 alkyl and/or E in formula $-\text{C}_n\text{F}_{2n}$ means a fluorine atom, are used.

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33. Use according to claim 30, wherein the compounds of general formula Ic, in which G represents lysine radical (a) or (b), are used.

34. Use according to claim 30, wherein the compounds of general formula Ic are used, in which Z means

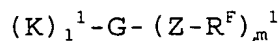


whereby γ represents the binding site of Z to radical G, and ϵ means the binding site of Z to perfluorinated radical R^F , and/or Y means $\delta - \text{CH}_2\text{CO} - \beta$, whereby δ represents the binding site to sugar radical R and β represents the binding site to radical G.

35. Use according to claim 30, wherein the compounds of general formula Ic are used, in which U in metal complex K represents $-\text{CH}_2-$ or $-\text{C}_6\text{H}_4-\text{O}-\text{CH}_2-$, whereby ω stands for the binding site to $-\text{CO}-$.

36. Use according to claim 30, wherein the gadolinium complex of 6-N-[1,4,7-tris(carboxylatomethyl)-1,4,7,10-tetraazacyclododecane]-10-N-(pentanoyl-3-aza-4-oxo-5-methyl-5-yl)]-2-N-[1-O- α -D-carbonylmethyl-mannopyranose]-L-lysine-[1-(4-perfluorooctylsulfonyl)-piperazine]-amide is used.

37. Use according to one of claims 1 to 7, wherein as perfluoroalkyl-containing metal complexes, the compounds with polar radicals of general formula Id



(Id)



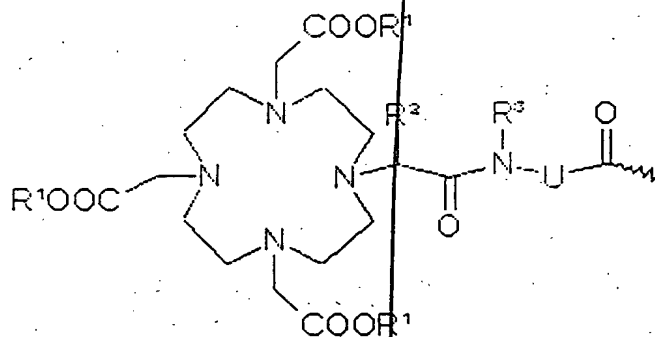
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Sub
Hb

in which

R^F is a perfluorinated, straight-chain or branched carbon chain with formula $-C_nF_{2n}E$, in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

K stands for a metal complex of general formula IIId,



(IIId)

in which

R^1 means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two R^1 stand for metal ion equivalents,

R^2 and R^3 , independently of one another, represent hydrogen, C_1-C_7 alkyl, benzyl, phenyl, $-CH_2OH$ or $-CH_2OCH_3$, and

U represents $-C_6H_4-O-CH_2-\omega-$, $-(CH_2)_{1-5}-\omega$, a phenylene group, $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega-$, $-C_6H_4-(OCH_2CH_2)_0-1-N(CH_2COOH)-CH_2-\omega$, or a C_1-C_{12} alkylene group or $C_7-C_{12}-C_6H_4-O$ group optionally interrupted by one or more oxygen atoms, 1 to 3 $-NHCO$ groups, 1 to 3 $-CONH$ groups

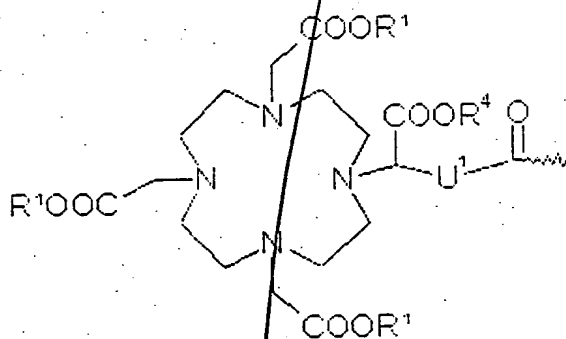
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and/or substituted with 1 to 3 $-(CH_2)_{0-5}COOH$ groups,
whereby ω stands for the binding site to $-CO-$,

or

of general formula IIIId

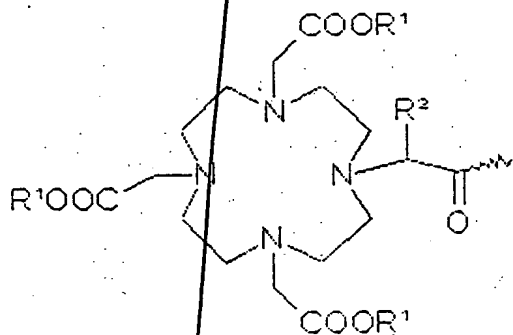


(IIIId)

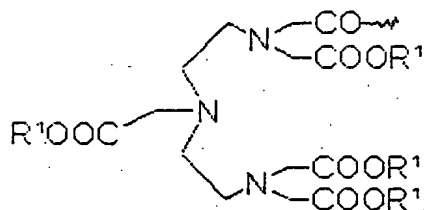
in which R^1 has the above-mentioned meaning, R^4 represents hydrogen or a metal ion equivalent mentioned under R^1 , and U^1 represents $-C_6H_4-O-CH_2-\omega-$, whereby ω means the binding site to $-CO-$,

or

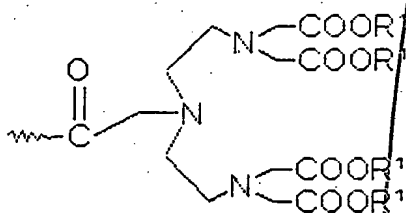
of general formula IVd



in which R^1 and R^2 have the above-mentioned meaning,
or of general formula VdA or VdB



(VdA)



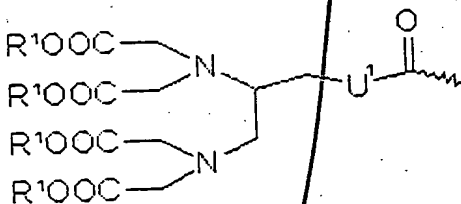
(VdB)

in which R^1 has the above-mentioned meaning,
or of general formula VId



(VId)

in which R^1 has the above-mentioned meaning,
or of general formula VIId



(VIId)

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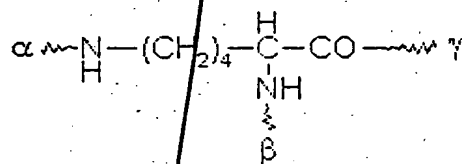
in which R^1 has the above-mentioned meaning, and

U^1 represents $-C_6H_4-O-CH_2-\omega-$, whereby ω means the binding site to $-CO-$,

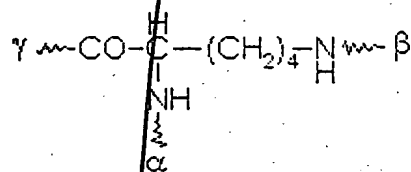
and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

G represents a radical that is functionalized in at least three places and is selected from the following radicals a) to g)

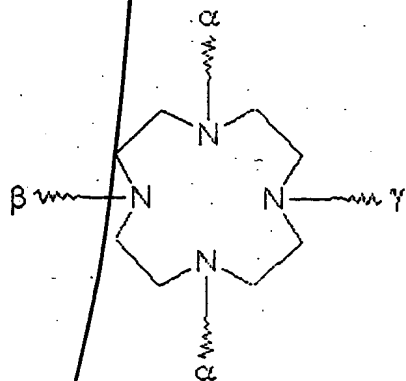
(a)



(b)

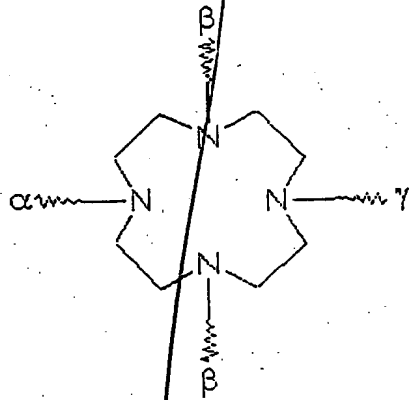


(c)

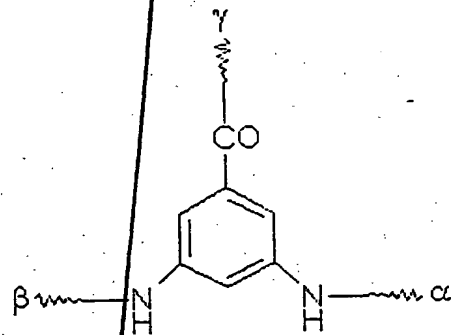


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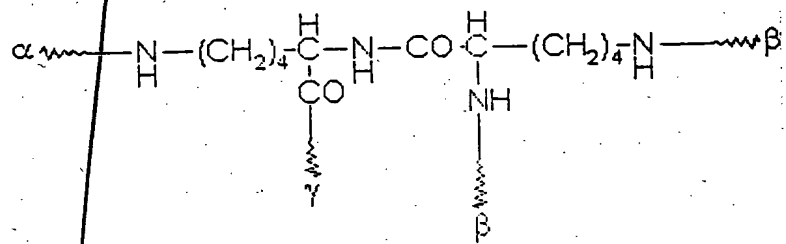
(d)



(e)



(f)

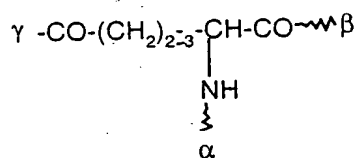


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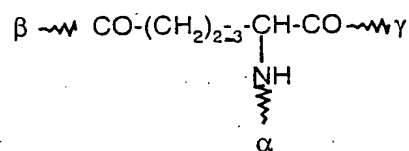
(g)



(h)

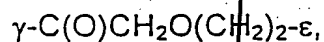


(i)



whereby α means the binding site of G to complex K, β is the binding site of G to radical R, and γ represents the binding site of G to radical Z

Z stands for



whereby γ represents the binding site of Z to radical G and ξ means the binding site of Z to perfluorinated radical R_f ,

R represents a polar radical that is selected from complexes K of general formulas IIId to VIId, whereby R^1

here means a hydrogen atom or a metal ion equivalent of atomic numbers 20, 23-29, 42-46 or 58-70, and radicals R^2 , R^3 , R^4 , U and U^1 have the above-indicated meaning,

or

means the folic acid radical

or

means a carbon chain with 2-30 C atoms that is bonded

to radical G via $-CO-$, or SO_2- or a direct bond and is straight or branched, saturated or unsaturated, optionally interrupted by 1-10 oxygen atoms, 1-5 $-NHCO$ groups, 1-5 $-CONH$ groups, 1-2 sulfur atoms, 1-5 $-NH$ groups or 1-2 phenylene groups, which optionally can be substituted with 1-2 OH groups, 1-2 NH_2 groups, 1-2 $-COOH$ groups, or 1-2 $-SO_3H$ groups,

or

optionally substituted with 1-8 OH groups, 1-5 $-COOH$ groups, 1-2 SO_3H groups, 1-5 NH_2 groups, 1-5 C_1-C_4 alkoxy groups, and

l^1 , m^1 , p^2 , independently of one another, mean integers 1 or

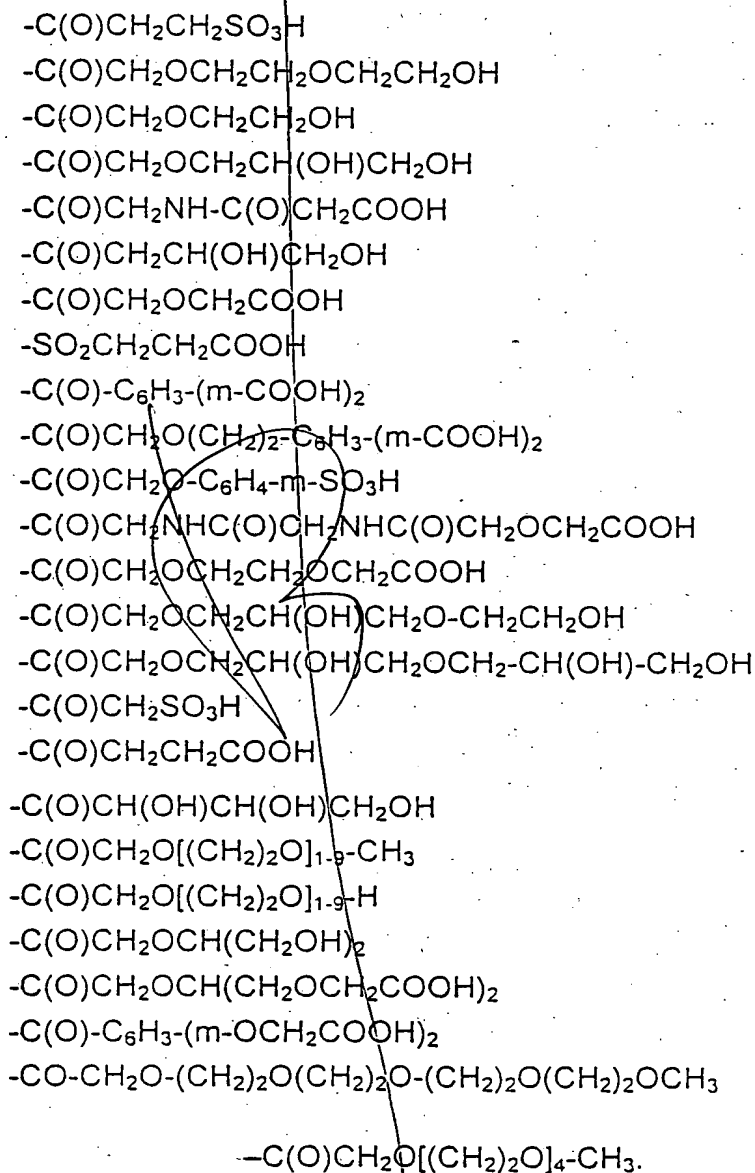
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are used.

38. Use according to claim 37, wherein the compounds of general formula Id, in which K stands for a metal complex of general formula IIId, IIIId, VdB or VIId, are used.

39. Use according to claim 37, wherein the compounds of general formula Id, in which polar radical R has the meaning of complex K, preferably complex K of general formulas IIId, IIIId, VdA or VIId, are used.

40. Use according to claim 37, wherein the compounds of general formula Id, in which polar radical R has the following meanings:



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preferably
are used.

41. Use according to claim 37, wherein the compounds of general formula Id, in which polar radical R is the folic acid radical, are used.

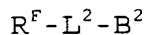
42. Use according to claim 37, wherein the compounds of general formula Id, in which G represents lysine radical (a) or (b), are used.

43. Use according to claim 37, wherein the compounds of general formula Id, in which U represents group $-\text{CH}_2-$ or $-\text{C}_6\text{H}_4-\text{O}-\text{CH}_2-$ in metal complex K, whereby ω stands for the binding site to $-\text{CO}-$, are used.

44. Use according to one of claims 37-43, wherein the gadolinium complex of 2,6-N,N'-bis[1,4,7-tris(carboxylatomethyl)-1,4,7,10-tetraazacyclododecane-10-(pentanoyl-3-aza-4-oxo-5-methyl-5-yl)]-lysine-[1-(4-perfluorooctylsulfonyl)-piperazine]-amide is used.

45. Use according to one of claims 1-7, wherein as perfluoroalkyl-containing metal complexes, galenical formulations that contain paramagnetic, perfluoroalkyl-containing metal complexes of general formulas I, Ia, Ib, Ic and/or Id and diamagnetic perfluoroalkyl-containing substances, preferably dissolved in an aqueous solvent, are used.

46. Use according to claim 45, wherein as diamagnetic perfluoroalkyl-containing substances, those of general formula XX



(XX)

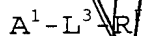
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in which R^F represents a straight-chain or branched perfluoroalkyl radical with 4 to 30 carbon atoms, L^2 stands for a linker and B^2 stands for a hydrophilic group, are used.

47. Use according to claim 46, wherein linker L^2 is a direct bond, an $-SO_2$ group, or a straight-chain or branched carbon chain with up to 20 carbon atoms, which can be substituted with one or more $-OH$, $-COO$, $-SO_3$ groups and/or optionally contains one or more $-O-$, $-S-$, $-CO-$, $-CONH-$, $-NHCO-$, $-CONR^9-$, $-NR^9CO-$, $-SO_2-$, $-PO_4-$, $-NH-$ or $-NR^9$ groups, an aryl ring or a piperazine, whereby R^9 stands for a C_1 to C_{20} alkyl radical, which in turn can contain one or more O atoms, and/or can be substituted with $-COO^-$ or SO_3 groups.

48. Use according to claim 46, wherein hydrophilic group B^2 is a mono- or disaccharide, one or more adjacent $-COO^-$ or $-SO_3$ groups, a dicarboxylic acid, an isophthalic acid, a picolinic acid, a benzenesulfonic acid, a tetrahydropyrandicarboxylic acid, a 2,6-pyridinedicarboxylic acid, a quaternary ammonium ion, an aminopolycarboxylic acid, an aminodipolyethylene glycolsulfonic acid, an aminopolyethylene glycol group, an $SO_2-(CH_2)_2-OH$ group, a polyhydroxyalkyl chain with at least two hydroxyl groups or one or more polyethylene glycol chains with at least two glycol units, whereby the polyethylene glycol chains are terminated by an $-OH$ or $-OCH_3$ group.

49. Use according to claim 45, wherein as diamagnetic perfluoroalkyl-containing substances, conjugates that consist of α -, β - or γ -cyclodextrin and compounds of general formula XXII



(XXII)

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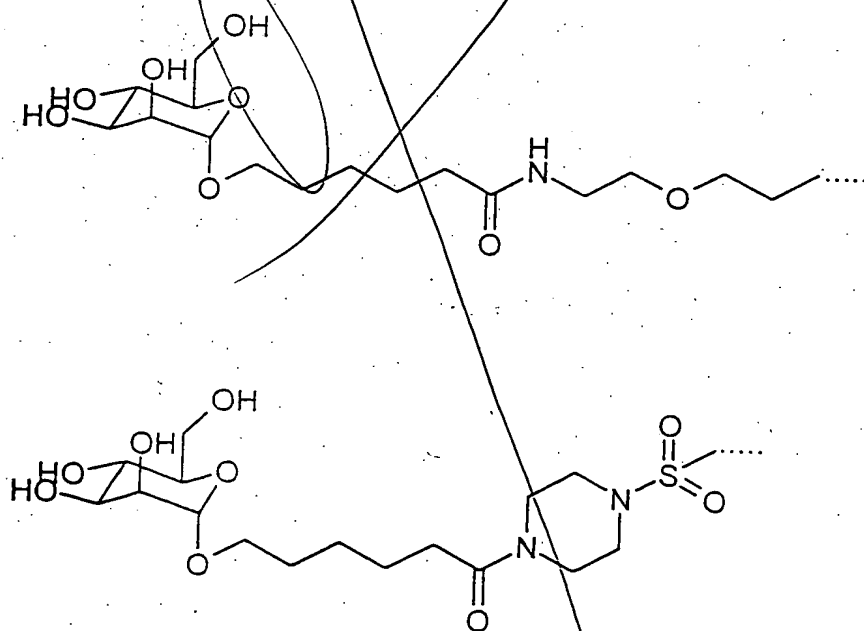
in which A^2 stands for an adamantane, biphenyl or anthracene molecule, L^3 stands for a linker, and R^F stands for a straight-chain or branched perfluoroalkyl radical with 4 to 30 carbon atoms, and whereby linker L^3 is a straight-chain hydrocarbon chain with 1 to 20 carbon atoms, which can be interrupted by one or more oxygen atoms, one or more $CO-$, SO_2- , $CONH-$, $NHCO-$, $CONR^{10}-$, $NR^{10}CO-$, $NH-$ or NR^{10} groups or a piperazine, whereby R^{10} is a C_1-C_5 alkyl radical, are used.

50. Use according to claim 45, wherein as diamagnetic perfluoroalkyl-containing substances, those of general formula XXI:

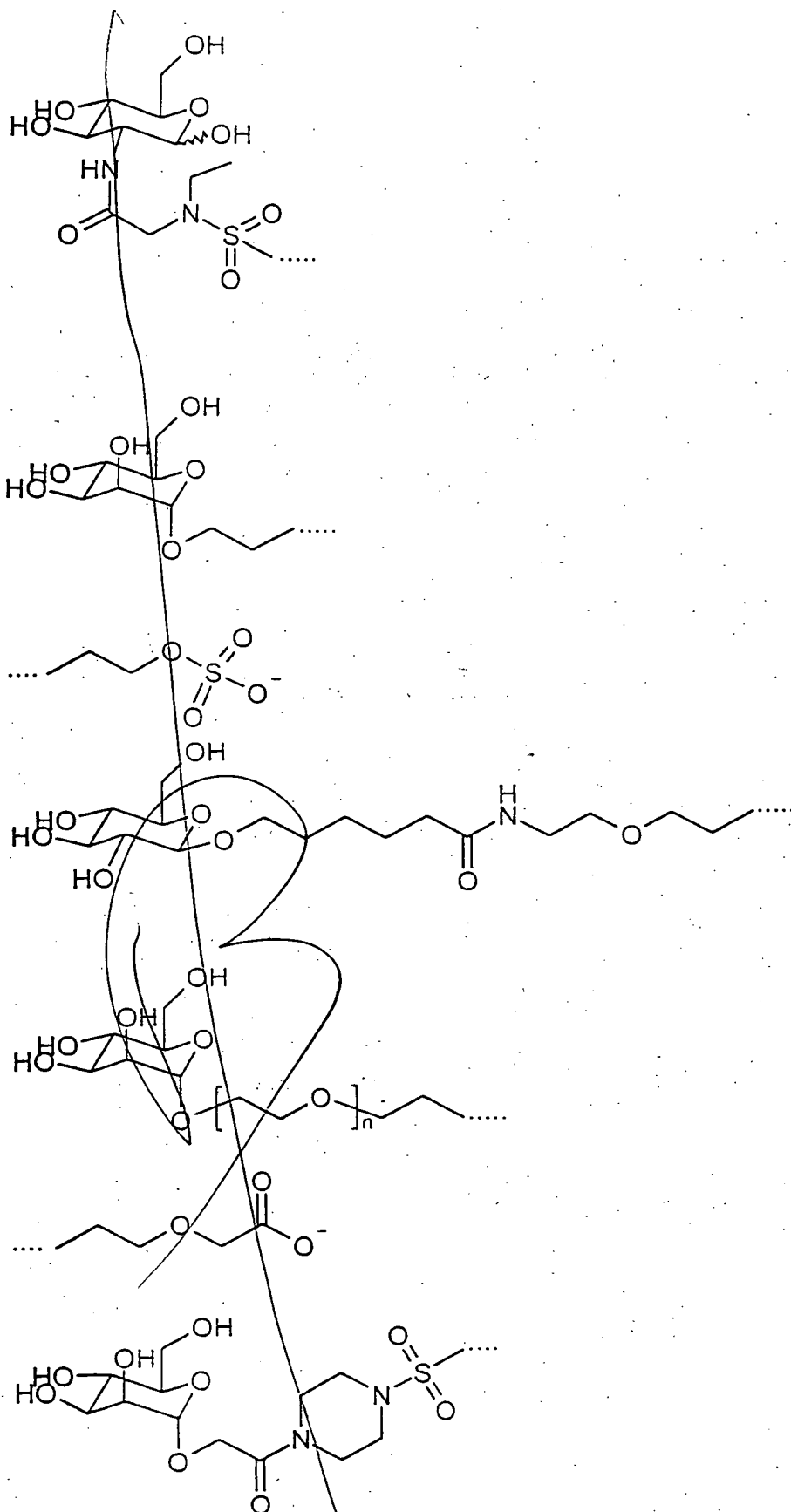


(XXI)

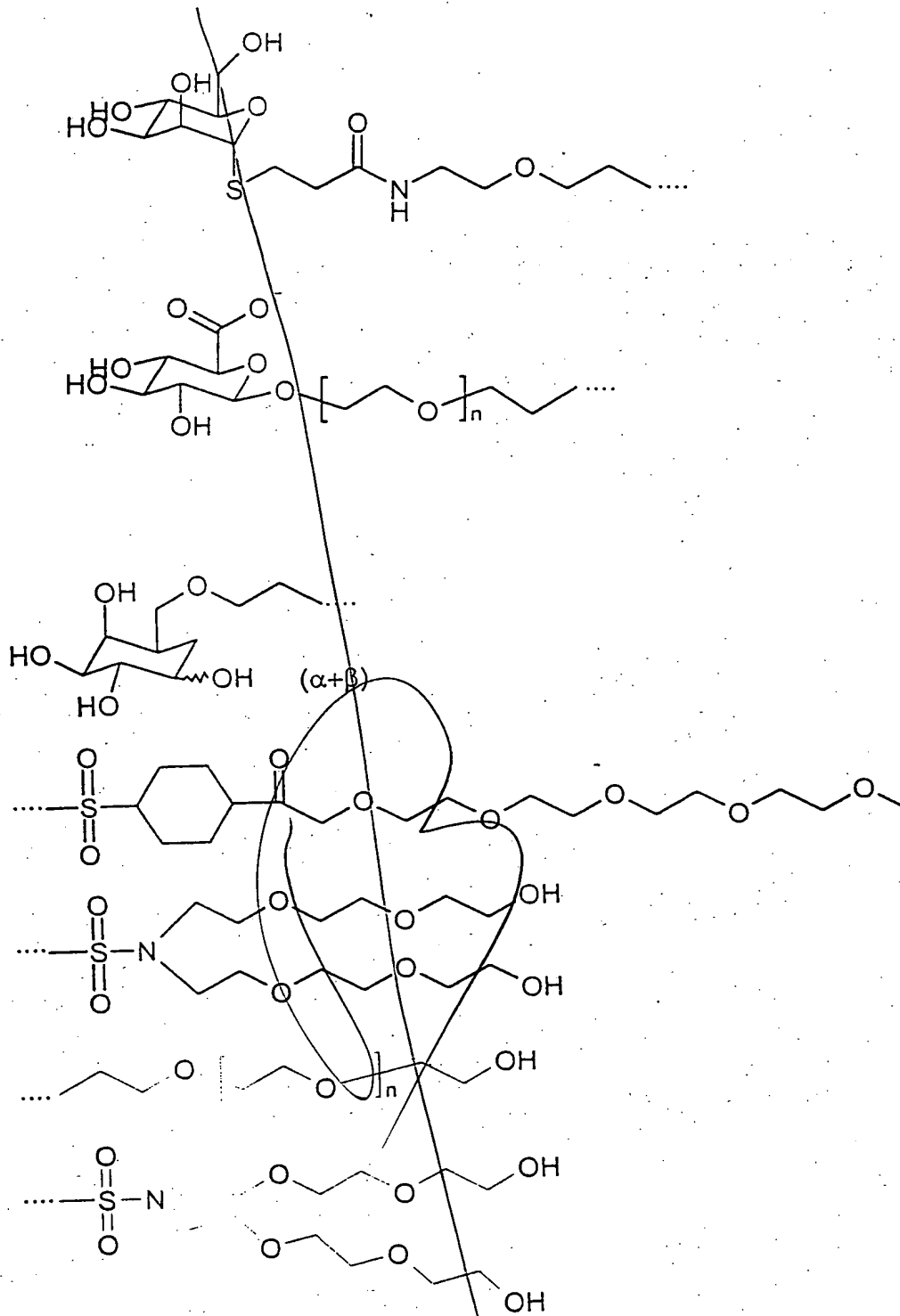
in which R^F represents a straight-chain or branched perfluoroalkyl radical with 4 to 30 carbon atoms, and X^1 is a radical that is selected from the group of the following radicals (n in this case is a number between 1 and 10), are used:



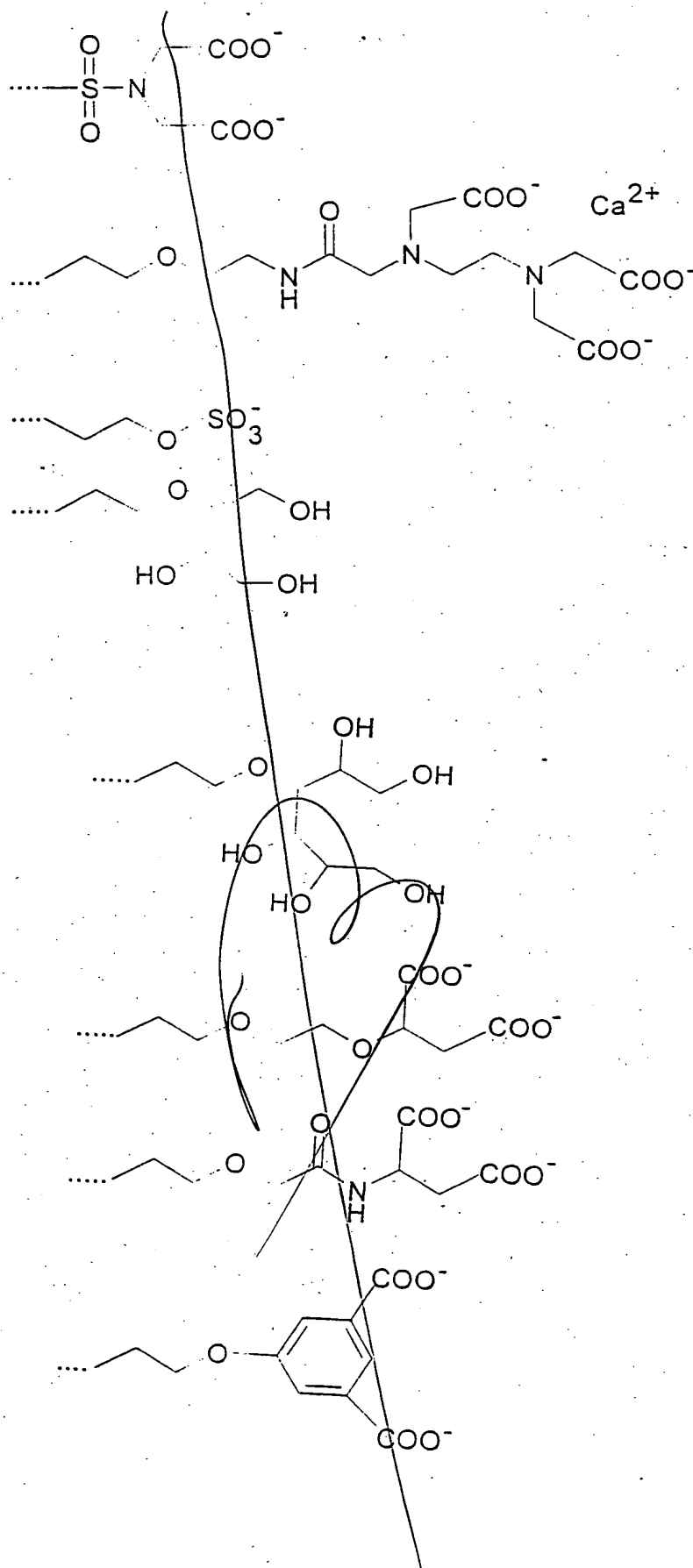
0925518 083001



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